

PATENT
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APPLICANT(S): Miller *et al.*
SERIAL NO.: 09/780,142 GROUP NO.: 1644
FILED: February 9, 2001 EXAMINER: Huynh, Phuong N.
TITLE *METHODS AND COMPOSITIONS FOR TREATING CONDITIONS OF
THE EYE*

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

*SUPPLEMENTAL DECLARATION OF
JOAN W. MILLER, M.D., UNDER 37 CFR 1.132*

I, Joan W. Miller, M.D., hereby declare as follows:

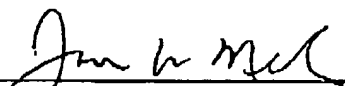
1. I am submitting this Declaration to supplement the Declaration I provided on September 19, 2005. The substance of my prior Declaration is incorporated by reference herein.
2. This Declaration is provided to supplement the record to describe experiments performed on a mammal using the combination of photodynamic therapy ("PDT") using verteporfin photosensitizer (also known as benzoporphyrin derivative, a tetrapyrrole derivative) and an antibody fragment that binds to vascular endothelial growth factor ("VEGF") for treating choroidal neovasculation.
3. The experiments were described in a paper that I co-authored entitled "Safety and Efficacy of Intravitreal Injection of Ranibizumab in Combination With Verteporfin PDT on Experimental Choroidal Neovascularization in the Monkey," Arch Ophthalmol, 123: 509-516, 2005 (the "Paper"). I understand that this Paper has been made of record as reference C171. The Paper reports an *in vivo* study on the safety and efficacy of intravitreal injections of an

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anti-vascular endothelial growth factor antibody fragment (known as ranibizumab) in combination with intravenous verteporfin PDT on experimental choroidal neovascularization in the monkey eye.

4. The results of the study presented in the Paper showed that "[n]o choroidal neovascularization leakage was observed in the eyes of animals treated with ranibizumab and PDT at day 21 or 42 after the start of the first treatment. [However, l]eakage persisted in eyes treated with PDT alone at 21 days (3 of 12 eyes) and 42 days (2 of 12 eyes). At all time points studied, the ranibizumab and PDT-treated eyes experienced better angiographic outcomes than the eyes receiving PDT alone." (Results section, page 509.)
5. The data from this study indicated that in a monkey model of choroidal neovasculture, the combination of verteporfin PDT and an antibody fragment that binds VEGF is more effective in treating choroidal neovasculture than verteporfin PDT alone.
6. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and that such willful false statements may jeopardize the validity of this application or any patent issuing therefrom.

Dated: January 9, 2006



Joan W. Miller, M.D.